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CHEMOSPECIFIC CARBONYL ALLYLATION BY ALLYLTIN REAGENTS. SYNTHESIS OF γ,δ-UNSATURATED ALCOHOLS

Yoshinori NARUTA, Satoshi USHIDA, and Kazuhiro MARUYAMA
Depatment of Chemistry, Faculty of Science, Kyoto University
Kyoto, 606

Allyltrialkyltin reagent reacted with carbonyl compounds in the presence of BF_3OEt_2 to give homoallyl alcohols. The yields were excellent and high chemospecificity was attained. By the reaction of 4-*tert*-butylcyclohexanone and 2-methylcyclohexanone trans alcohols were stereoselectively obtained in 92 and 94% isomeric purity, respectively.

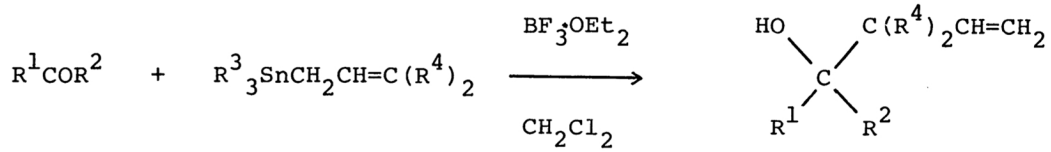
The development of versatile methods for forming carbon-carbon bonds under mild conditions is a central objective of synthetic organic chemistry. Especially chemospecific alkylation is demanded for the synthesis of polyfunctional natural products.

Marked reactivity of allyltin compounds to electrophiles has been elucidated to be due to the hyperconjugation (or σ-π) of the carbon-tin bond,[1] and appears to us to be a particularly attractive vehicle for the synthetic elabolation of functionalized alcohols. The addition reaction of allyltin to carbonyl group polarized by strong electron withdrawing group (e.g. CF_3, CCl_3)[2] was reported to give homoallyl alcohols,[3] although the reaction was limited to electron deficient carbonyl compounds.

Previously we attained the chemoselective allylation of carbonyl group of 2,3-dihydro-2,3-epoxy-1,4-naphthoquinone in the presence of BF_3OEt_2 with complete preservation of the epoxy group.[4] This characteristic feature was extended to the selective allylation of bifunctional carbonyl compounds, and a new synthesis of homoallyl alcohols. These chemospecific reactions have never been attained by the usual organometallic alkylating reagents (e.g. RMgX, RLi, R_2Cu, etc.).[5,6] The results are summarized in Table 1. Even in the presence of Br, NO_2, CN, and OH substituents the allylation on cabonyl groups is successful (Entry 7, 8, 9, and 10).

In a typical experiment, to a dichloromethane solution of benzaldehyde (1.0 mmol) was added BF_3OEt_2 (2.0 mmol) and afterward allyltrimethyltin (1.1 mmol) at -78°C under N_2. The resulting mixture was allowed to warm slowly to 0°C (1-2 h). After usual work-up, purification by preparative TLC gave the desired homoallyl alcohol: 92%. In other reactions every homoallyl alcohol is isolated by preparative TLC on silica gel and its structure was identified by spectroscopic methods and/or elemental analysis. In the reaction of aldehydes with nitro, or hydroxy groups, use of excess amount of BF_3OEt_2 (3-4 equiv.) gave higher yields. This is suggestive that the competitive complex formation between the carbonyl group and other functional groups with BF_3 may arise. The reaction with acid labile aldehydes provided desired yields by quenching the reaction mixture at a low temperature (-70°C), while under the standard reaction conditions these aldehydes resulted in the formation of a large amount of polymeric products or

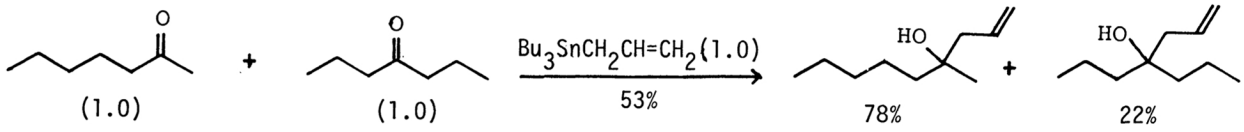
of a complex reaction mixture (Entry 10, 11, 12, and 13).

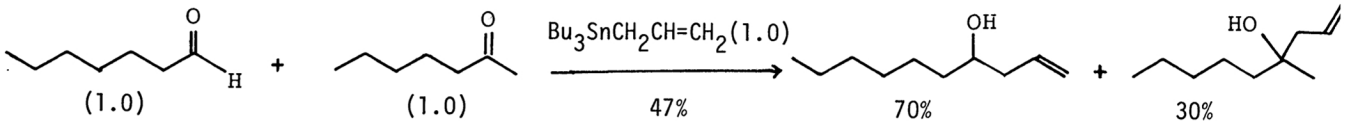


R^1=Alkyl, Aryl R^2=H, Alkyl R^3=Me, Bu R^4=H, Me

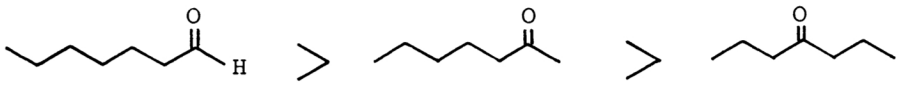
N-Methylpyrrolecarbaldehyde was recovered quantitatively without reaction in spite of the presence of an excess amount of BF_3OEt_2.

Interestingly, the allyltributyltin reagent can discriminate 2-heptanone from 4-heptanone, and heptanal from 2-heptanone.



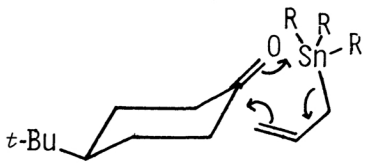


The relative reactivity for the allyltributyltin-BF_3 reagent is in the following order;



In general, aldehydes were more reactive than ketones, and terminal ketones were allylated more easily than inner ones. This chemoselectivity could originate from the facility of attack of the allyltin reagent to the reaction center ---- carbonyl group.

To obtain the general feature on the stereoselective points of view of the reaction, we investigated the allylation of cyclohexanone derivatives, e.g. 4-*tert*-butylcyclohexanone which is effectively "locked" in a single chair conformation and is known as an excellent probe for judging the stereoselectivity of a reagent.[7] *The highest stereoselectivity* of the reported so far was attained by the present reagents (Entry 15, 16, and 17). The use if allyltributyltin (2.3 equiv. to ketone) instead of the trimethyl derivatives recorded higher stereoselectivity (92% *trans*-alcohol) and higher yield (93%). This remarkable improvement in stereoselectivity is presumably a reflection of the bulkiness of allyltin reagent around the reaction center. We have also observed a similar improvement in stereochemical control for the allylation of 2-methylcyclohexanone. While the factors influencing to the stereochemical control are not fully analized, the coordination such as 1 in the transition state may favor the



1

Table 1. Reaction of Carbonyl Compounds with Allyltin Reagents

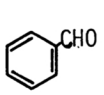
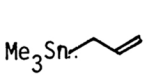
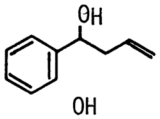
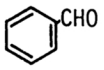
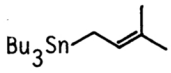
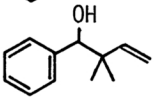
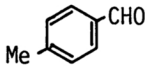
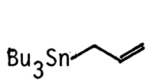
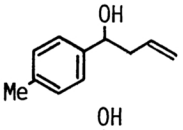
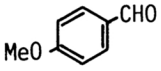
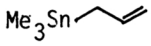
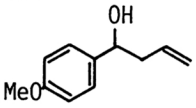
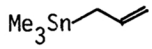
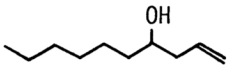
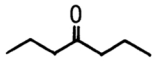
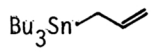
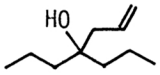
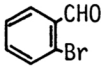
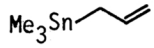
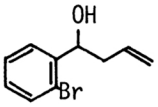
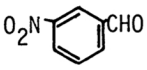
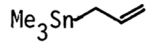
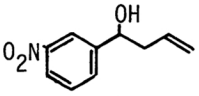
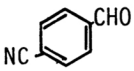
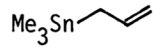
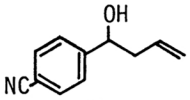
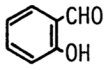
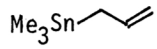
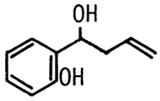
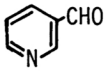
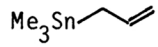
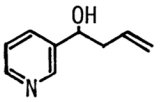
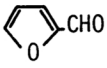
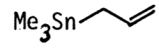
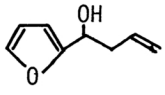
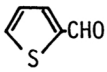
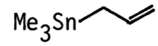
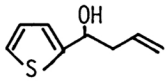
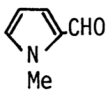
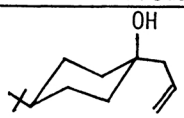
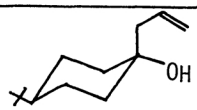
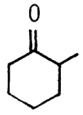
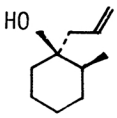
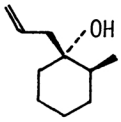
Entry	Substrate	Allyltin (equiv.)[a]	BF_3OEt_2 (equiv.)[a]	Reaction condition[b]	Product	Yield (%)[c]
1		 (1.1)	2.0	A		94 (92)
2		 (1.2)	1.0	A		93 (90)
3		 (1.1)	3.0	A		87 (80)
4		 (1.1)	2.0	E		66 (42)
5		 (1.2)	2.0	A		76 (73)
6		 (2.3)	2.0	A		99 (95)
7		 (1.3)	4.0	B		99 (94)
8		 (1.25)	2.5	C		99 (68)
9		 (1.4)	4.0	A		99 (85)
10		 (1.45)	4.0	D		80 (70)
11		 (1.5)	4.0	D		99 (86)
12		 (1.3)	3.0	D		88 (72)
13		 (1.5)	3.7	D		92 (90)
14		(1.5)	4.0	D	n.r.	—

Table 1 (Continued)

Entry	Substrte	Allyltin (equiv.)[a]	BF_3OEt_2 (equiv.)[a]	Reaction Condition[b]	Product		Yield (%)[c]
15		Me_3Sn  (1.2)	2.0	A	 85[d]	 15[d]	(48)
16		Bu_3Sn  (2.3)	2.0	B	92[d]	8[d]	(93)
17		Bu_3Sn  (1.3)	2.0	C	 94[d]	 6[d]	(71)

[a] Molar ratio to substrate. [b] A; In CH_2Cl_2, -78∿0°C, for 1.5 h. B; In CH_2Cl_2, -20°C, for 0.5 h, and then 0°C. C; In CCl_4, -20°C, for 0.5 h, and then 0°C. D; In CH_2Cl_2, -78∿-70°C, for 0.5 h. E; In CH_2Cl_2, -78°C for 1 h, and then -50°C. [c] Yield in parentheses is of isolated product. Others are estimated by NMR by using cis-1,2-dichloroetylene as an internal standard. [d] Product ratio was determined by g.l.c. and NMR.

equatorial attack of the allyl group (steric approach control).[7,8] The present reaction clearly provides a novel method to introduce an allyl group chemospecifically and stereoselectively to a carbonyl group.

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References and Notes

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